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Pécs, 1953

The main issue:

The morphology and pathology of connective tissue and interstitium

DEVELOPMENT OF THE CONNECTIVE TISSUE AND ITS CAPACITY OF TRANSFORMATION

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(A Review)

The morphology of the connective tissue, its chemistry and its cellular elements, the problem of the evolution of the living substance, the reticulo-endothelial apparatus, fibre formation, the problems of transformation of the connective tissue, its differentiation and dedifferentiation, etc., cannot all be taken up in this review. Two problems will only be discussed: the closely related problems of development and transformation. I have chosen these two points from among the ones mentioned, since in my opinion they are at present of the greatest interest for all researchers.

Before discussing the transformation of embryonal connective tissue it must be established whether or not the material generally termed embryonal connective tissue is a kind of connective tissue. The mesenchyma, which has been termed embryonal connective tissue by many an author, is neither a young nor any other kind of connective tissue, but an undifferentiated tissue from which connective and also other kinds of tissues, such as cartilage, bone, muscle, bone marrow, etc., may develop through differentiation. The pluripotence of the mesenchyma is an established fact. On the other hand, much controversy has arisen in respect of the factors influencing the differentiation of the mesenchyma. The dialectical approach demands to point to the inherent factors harboured by the cells since it is they which constitute the framework within which differentiation can take place. The mode of differentiation is under the influence of the functions and the needs of the organism.

The first question which arises is how the various fibres, the collagenic, elastic, and argyrophilic fibre develop and whether they are capable of being transformed into each other. The question is still unsettled. Most of the examinations carried out with biological tissue have shown that the development of the fibres is independent of each other. On the other hand, authors working with pathological material could observe transitional stages.

As to the collagen fibres, it has been accepted that they can be formed at any place where, under normal conditions, cells of mesenchymal origin, i.e. fibroblasts are present. The assumption is warranted that the fibrils once developed — polypeptide chains — may, under the influence of the basic substance, the tissue fluids, and physical factors undergo thickening, longitudinal growth, or reproduction. Under experimental conditions the fibrils may be dissolved and again formed into fibres. No evidence has been brought forward regarding the problem whether collagen fibres could be formed in areas where fibroblasts never had been present.

The binding substance too plays a prominent role in the development of collagen bundles and their structure. According to certain data (B) the elementary fibre deprived of its binding substance, the electron micrograph appearance of which is known, is elastic and distendable.

As regards elastic fibres and membranes all authors who have ~~discussed~~ their development stand for their cellular genesis (cf. the lecture to be held by the present author at this same congress).

The elastic substance is probably the same as the binding material, the latter stains with resorcin-fuchsin and is soluble by elastase.

The question has been raised whether or not elastic elements can be formed without cells. The existence of such a process has been repeatedly assumed but no conclusive evidence has been brought forward as yet.

Another unsettled problem is the difference between argyrophil, collagen, reticulin, and collagen fibres. The binding substance deposited by the fibril is undoubtedly different with the single kinds of fibre, what is known is whether the elementary fibril itself is identical or similar with the binding substance, which has an essential role in the behaviour of the fibre. It is responsible for the variability of the argyrophil fibre that this fibre is readily capable of swelling or of becoming dissolved.

Many authors regard the theory more progressive that the fibres are formed by the basic substance independently of cells. This theory is partly due to the fact that until quite recently all cells, even the majority of the bone cells (e. g. chondroblasts), were held to be strictly determined. While the fix determination of cells was still the view generally adopted, Rakke, ~~Björk~~ and Husella, already claimed that the intercellular substance could give rise to the evolution of a fibril system along the lines of tension. Beside the cellular theory a new thesis has been developed considering that environmental conditions may take part in directing the evolution of intercellular substance and much evidence favouring this view has been produced. At that time the experimental and embryological basis was still insufficient for demonstrating that both function and environmental conditions have a decisive role in the determination and differentiation of the cell proper. Since then it could be proved that differentiation of granulation tissue depends on the action of various functional and environmental conditions, so that in traction connective tissue develops, while in pressure, cartilage. Our experiments have demonstrated that it is possible to change not only the intercellular substance but also the determination and differentiation of cells by changing environmental conditions.

It is not the notion of the cell itself which has been debated by the progressive theory but the view according to which every cell is determined by inheritance. Fifty or twenty five years ago the opinion seemed acceptable that influences act only upon the intercellular substance. Presently a ~~hard~~ stop can be made in regard to the cell. There are facts to show that cells play a prominent part in fibre formation. Since the cells are regarded as accessible to different influences rather than determined *a priori*, there is no obstacle to recognise that in the formation of fibres not only the basic substance, the whole organism, special functions and environmental effects (e. g. physical effects) have their own role, but also the cells, especially those cells the differentiation of which is equally under the influence of environmental effects.

As to the connective tissue cells apt to become transformed, it may be seen from the literature that, according to their localization in various organs

elements of connective tissue, and the development of granulation tissue. The granulation tissue is formed by the breakdown of connective tissue elements, and it is composed of a variety of different elements. The structure and function of the granulation tissue are determined by the presence of these different elements, and the relative number of each element.

Thus, a more progressive view has taken the place of the old concept according to which the cells of the connective tissue could develop into various types of cells, and reserve cells could form nothing but connective tissue. The components of tissue were possibly various such reserve cells, storage and multiplying elements of tissue were possibly various such reserve cells. The old concept of the source of the cell was too simple and dogmatic. Cells were considered as partly determined in both differentiation and topographical location. We regarded the cells as definitely bound to a certain place and disregarded the capacity of the cell to move position. If one cell was observed at a site, it was assumed we did not know if it was possible that cells had been there at an earlier time, one hour, one day, or one month ago.

From among the connective tissue cells, the elements of granulation tissue deserve special attention with respect to their capability of transformation. The granulation tissue differs from embryonic mesenchyma, and its elements may vary continually, elongating and so forth. The elements are undifferentiated and undetermined. As far as potential and so freely changing their position they are the students of the embryo, and the embryo is not differentiated. There are the differentiated reserve cells (e.g., chondroblasts, fibroblasts) which are impossibly dependent, nor fastened to a certain place.

It is the factors and the milieu which exert a decisive influence on the determination, differentiation, and motion of granulation tissue elements. It would, of course, be important to define the actual environmental factors. Such other factors as chemical, physical, or complex biological characters do not appear to be involved. Surface action, special physical effects, such as traction, pressure, or strain, confronting increased functional demands, may also play a role.

What possible influence on the evolution, regeneration, or new differentiation can be connected with?

The question can be divided in several points:

- (a) Is it possible that the formation of granulation tissue, or on its differentiation to connective tissue be influenced?

Ad (a). The incitement of granulation tissue to be influenced by various chemical, physical, and biological stimuli has already been, and according to the results of Fischer-Went, should best be mentioned in this regard.

Further investigation in this field would be most promising. In the experiments of Chevremont the application of choline resulted in a histiocytic differentiation of granulation tissue elements. Laroche et al.¹⁰ results referring to the reticuloendothelial apparatus lie outside the field of the present review. The appearance of granulation tissue may be influenced in a negative sense by the administration of cocaine.

Ad (b). Is it possible to influence the differentiation of granulation tissue into connective tissue? This question has been well known since Jeney and Torn,¹¹ fundamental experiments several years confirmed by numerous authors.

100 300 600

In the differentiation of connective tissue, the main role is played by the granulation tissue. Before a permanent form is given to the connective tissue, the granulation tissue is the precursor of the connective tissue. It is the granulation tissue which takes partake in building up the fibres.

The differentiation of granulation tissue may be influenced in two ways. First it may be influenced in practice by exerting influence upon the granulation tissue. The fraction exerted on living matter gives rise to a transformed tissue, the properties of which are still unknown, but in some cases a change of properties may be seen taking place. The differentiation of granulation tissue towards the direction of regional environmental effects, and it is possible to regulate the differentiation of granulation tissue. Collagen is formed at the transition to living tissue, as a result from intermittent traction provided that the basic conditions are met. Elastin, vitamins, enzymes are added, and gelatinous substances are removed.

The influence of the nervous system on the granulation tissue and formation of the connective tissue has been known since the work of Hahn, Dreser, and Pavlov. As to its mechanism, the neurovascular theory has been advanced. Recent investigations (Babai and his associates) have shown that supporting tissues are also under the influence of the nervous system through the mediation of the salt metabolism.

The following practical conclusions should be drawn from the above:

- Since it is possible to influence changes and directions of the function of the developing tissue and its environment, the possibility of influencing the cells of granulation tissue is given.

- Granulation tissue may be mobilized.
- At a given place, the elements of granulation tissue may be determined in a direction other than the previous one.
- Thus differentiation of the granulation tissue cells may be mobilized may be influenced in a way that they might meet the aims of healing.

Further results are expected from Hungarian workers studying the capacity, potency, determination, differentiation and dedifferentiation of cells. In this field the study of function, the examination of the chemical, physical and general biological environment, and the realization of a biologic synthesis are the main items of experimental work.

Increasing attention should be paid to the evolution of cells from living protein.

In continuation of the fine results in the discovery of elastase etc. by Babai and Banga, our young collaborators are expected to achieve further results relative to the detailed structure and chemistry of the basic substance. This work should be continued with the aid of the electron microscope. First of all histogenetic examinations should be completed by the electron microscopic method, as observing developing fibres in the course of their evolution will greatly assist in understanding and interpreting their structure.

Studies as to the transformation of fibres are also expected to be carried out in this country.

Summarizing in one sentence our present view regarding the evolution of connective tissue and its capacity of transformation we are greatly ahead of the old concept that the connective tissue is nothing more than a supporting tissue. Connective tissue is an ever-changing and transforming tissue containing many granulation elements, undifferentiated, undetermined, pluripotent, freely moving derivatives of postembryonal mesenchyme.

Granulation tissue harbours enormous potential forces. By a planned bringing of the function and the environmental conditions into proper directions ourselves must transform the inhibited granulation tissue to the very kind tissue needed by the diseased organism.

PATHOLOGY OF THE CONNECTIVE TISSUE

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(A Review)

Until the first years of this century it had been believed that connective tissue has little importance in comparison with parenchyma. Virchow's work in the previous century had consisted essentially in the evolution of Morgagni's localization principle, according to which the course of diseases should be observed in the parenchymal cells. Although the significant role of connective tissue elements in inflammatory processes and the growth of tumours had been recognized, the intercellular substance had been considered non-living. The attention of pathologists had therefore became focussed to the cells of the connective tissue, the reticuloendothelial apparatus (Aschoff, Zavarzin), the physiological system of connective tissue (Bogomolets), and the connective tissue fibres (Luna). The relation between extracellular substance and pathological conditions had been pointed out first by Spiess (1857), and later by Stricker. In their wording, the pathological changes of cells must of necessity be reflected by the basic substance. Heidenhain already claimed that cell and intercellular substance are equivalent. Hueck emphasized that the intercellular substance represents, in a physico-chemical sense, a structure more vital than the cell itself. Huzella, in contrast with the adherents of cellular pathology, pointed out the importance of intercellular pathology and developed his theory on the *oblastomotor micromechanism* of the intercellular fibre apparatus. In the view of Rindfleisch, the metabolism, growth and excitability of cells depend on the connective tissue representing an organ of adaptation and a mediator between the parenchyma and its vessels; the capillary membrane would represent the endothelial borderline layer of the connective tissue. In his well-known *sinicular pathology*, Schade states that the basic substance of the connective tissue plays a prominent role in the regulation of tissue permeability. In the opinion of Eppinger and his pupils, Schürmann, and MacMahon, changes in tissue permeability are due to changes occurring in capillary permeability. The oedematous imbibition of the intercellular substance may in severe cases result in necrobiotic and sclerotic processes. The investigations of Lepechinskaya have made it possible to understand numerous vital processes hardly known before and it due attention is paid to the leading role of the nervous system, light will be thrown upon numerous problems in the pathology of connective tissue.

From among the widely branching problems of the pathology of connective tissue, the present review will discuss the formation and changes of the basic substance, the so-called collagen diseases, the hormonal effects, and the nervous correlations.

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The amount of the mucopolysaccharides in the connective tissue, this large hyaluronic acid, the estimation of the concentration of the connective tissue. The mucopolysaccharides consist of protein and mucopolysaccharides. According to Malmstrom and Duran Beyoul (1960) the total carbohydrate of the mucopolysaccharides by Malmstrom and Palmer (1960) is hyaluron sulphate and chondroitin sulphate. According to the enzymatic examinations it can be seen that the mucopolysaccharides have a protective tissue structure and basal membrane system. The mucopolysaccharides being situated in the de- mineralized state react pseudouridine blue when exposed to the hydrolysis with pseudouridine. They are found to be digested under the action of enzymatic bromochromic acid. According to Sylven (1956) and Sylven (1960) the mast cells and fibroblasts of the connective tissue have the same properties. It is also known that the mast cells of the connective tissue have a relation between the amount of metachromasia and the number of cells. According to Holmgren, Wikander and Torpe (1958) the mast cells are produced by the mast cells. Starting from the fact that the proteins in the connective tissue are not digested by hyaluronidase. A few hours after the removal of the connective tissue the mast cells produce a protease or of hyaluronidase. According to Holmgren and Wikander (1958) it is suggested that the mucopolysaccharides are secreted by the mast cells and the connective tissue by Kothlker and Klempner (1958) may be dependent on the amount of the connective tissue. The results of Devceny and Holmgren (1958), of Sylven (1956) and of Fawcett, Jeney and Torpe and Daniell and Klemperer (1958) indicate the formation of the basic substance a proportion of which is the hyaluronic acid. On the other hand Hess and McDonald do not consider the hyaluronic acid important. There are numerous reports on quantitative changes in the amount of thyrotropic hormone and oestrogen. Ludwig and Riedel (1958) treated with testosterone, that is the combination of the two substances was deposited and the secretion of the thyroxine increased. The secretion of the thyroid and Ammonium formic acid supports Sylven's view. In the connective tissue resembling peritoneal muscle with myofibres, the mucopolysaccharides are various enzymes such as cathepsin, chymotrypsin, trypsin, hyaluronidase, etc.

The effect of various enzymes used to combat infection, infection and toxicosis, may consist of a substance result in the formation of some staining properties, e.g., hyaluronic acid and fibrin. Depolymerization is brought about by fibrolytic or enzymatic action. The chemical similarity of these substances suggests the validity of the assumption that the former may exert similar effects. Enzymes ACTH and Cortisone also exert a regulatory way they are capable of inhibiting or stimulating the action of the depolymerizing enzymes, being all made of basic collagenase and elastase (14). Because of the posting-mucopolysaccharide effect of cortisone should be mentioned, it can be asked whether the hydrolyzing effect of the enzyme is suppressed. The fact, on the other hand, that the enzyme becomes markedly more active at the same time

Specific antihyaluronidase may be demonstrated in the urine of patients with collagen diseases. The change of the viscosity of the following the action of hyaluronidase, production, polymerization and depolymerization of the mucopolysaccharides of the basic substance of connective tissue. An increase in the amount of hyaluronic acid could be demonstrated in numerous pathological conditions. Dr. G. H. Ross and S. Lert have produced experimental exophthalmos in the adrenalectomized guinea pig by treating them with the chondrolytic enzyme. At the same time they have found a marked increase of mucopolysaccharides in the connective tissue of the orbit. It is a well-known fact that the hypertrophy of the thyroid gland and also the hypofunction of the thyroid gland is accompanied by changes in the metabolism of the connective tissue mucopolysaccharides. These changes are most probably not only of a quantitative but also of qualitative character. Hyaluronic acid is an important factor also in Ross's serum inflammation. It is known from the studies of Rusznayak, Holdi and Szabo that certain substances acting similarly to hyaluronidase may lead to depolymerization of the basic substance of the connective tissue. In this way the permeability of both the connective tissue and the lymph vessel walls is increased and the penetration of colloids and corpuscular elements into the lymph vessels is facilitated. The chondrolytic substance present in the growth zone of malignant tumors originates from the mucopolysaccharides of the basic substance on the action of a hyaluronidase-like enzyme produced by the tumor. In the opinion of Simonetta, the concept of mucous and myxoid degeneration of tumors needs revision since part of these substances is derived from the stroma rather than the parenchyma. The increase in permeability due to the effect of hyaluronidase facilitates the nutrition and spreading of the tumor. In our belief, the equilibrium between hyaluronic acid and hyaluronidase is the final result of intracellular nervous and humoral reactions.

Depolymerization products of the connective tissue basic substance develop in an essentially identical manner. In the early stage they are all oedematos and mucinous; they appear in the extracellular connective tissue; their staining reactions are identical and mutual transformation may occur. **In sclerosis** a homogeneous, refractive, presumably non-functioning matter is formed without previous granulation. This is the final stage of serum inflammation. Hyalin too is a refractive, homogenous, inabsorbable substance part of which resembles the collagen fibre whilst the rest contains tyrosine and tryptophane. Its substance is of globulin character which can be demonstrated in chronic inflammation by histological methods. It may undergo absorption or become deposited. Aptly distinguishes amyloid and paramyloid, both contain mucopolysaccharides resistant to hyaluronidase. In the view of Randerath, they develop in consequence of a general disorder of protein metabolism in the course of which pathologic heterogeneous proteins may be formed. Romhanyi has shown that amyloid is a crystalline substance possessing a characteristic micellar structure. As serum proteins, with the exception of fibrinogen, do not occur in crystalline form, amyloid is made up of changed serum protein. **The mucoid degeneration** of Falabek's mucinous oedema, marked mainly by an increase in the amount of hyaluronic acid, occurs in numerous diffuse and focal diseases of the connective tissue and may be produced by protracted administration of desoxycorticosterone acetate, estrogen or androgen. **Mucoid degeneration** is not a specific change. **Ebneroid** is a homogeneous, anisotropic, strongly refractive cellular substance which according to S. Kellert consists

of altered collagen damaged connective tissue substance and then occurring into the inflamed area. According to Abschüller and Vogel, the bond originates from the acid mucopolysaccharides of the basic substance precipitated by an alkaline matter of protein character. Rücke of the opinion that fibrinous necrosis is a local manifestation of anaphylaxis. In particular, during after mucoid degeneration, fibrinous necrosis may undergo coagulation, hyalinization, sclerosis and occasionally also amyloidosis. Under the microscope, swelling of the collagen fibres, separation and fragmentation of the fibres and eosinophilic transformation of the basic substance and the fibres may be observed. It is for this reason that Klemperer held the condition typical of the collagen. On the other hand, Wolpers could demonstrate by means of the electron microscope that the fibres remain intact. Assuming that collagen vasomotorism represents a state of oversensitivity, Klinge attempted to explain by a similar mechanism certain other diseases characterized by a fibrous change of the connective tissue, such as periorbititis nodosa, dermatitis herpetiformis, malignant nephrosclerosis, thrombangitis obliterans, E.D., sarcoid, etc., etc. Fibrous change of collagen may, however, occur also in conditions in which there is no hypersensitivity. Other observations emphasize the effect of mechanical factors and, in the early stage of vascular lesions, the primary injury of the smooth muscle in the vessel wall. In collagen disease all the connective tissue elements are damaged - this is why in his later papers Klemperer himself suggested to employ the term mesenchymal instead of collagen disease. Since the general mesenchymal lesion is attended by an increase in globulin produced by the plasma cells, Klemperer holds the condition to be of gammapathia characterized by fibrinous degeneration, denaturation of the basic substance, and increase in the globulin level. The secondary reaction, however, varies with the single morbid patterns.

The standpoint of Klinge, who distinguished various disease groups on basis of fibrinous necrosis, cannot be maintained. Klemperer, who first used the term collagen disease, has also modified his view with regard to the fact that the condition under consideration is neither a common disease nor the isolated lesion of the collagen substance. Further the common morphological basis allows no conclusion to a common genesis and so many problems are still unsettled that there is no foundation yet to evolve a synthesis.

As regards the pathogenesis of inflammation, only the influence of the pituitary and adrenal hormones upon the reaction of the connective tissue will be discussed with special regard to the changes of the basic substance of the connective tissue. It is well known that the reaction of the connective tissue is decreased by cortisone and ACTH. At the same time capillary permeability, hyaluronidase effect, oedema and pus formation are also diminished. Heilmeyer claims that also the resistance to infection is decreased as consequence of a decreased production of antibodies. In this way a phase of negative energy may set in. According to Heilmeyer these reactions may be elicited also by endogenous hyperthyroidism. These effects, however, cannot be produced by cortisone or ACTH by themselves, since in Addison's disease similarly as in adrenalectomized animals, no hyperergic reaction occurs although the cortisone effect is missing. On the other hand, high doses of desoxy-corticosterone acetate are followed by a mesenchymal reaction in the experimental animal. It was Selye who has shown that cortisone elicits an increase in the secretion of desoxy-corticosterone acetate and in the production of somatotrophic hormone (STH).

The following table gives the results of the experiments made at the University of California, Berkeley, on the effect of the addition of various organic acids on the growth of *Candida* and *Aspergillus*. The cultures were grown in 100 ml. flasks containing 20 ml. of a medium consisting of 10 g. yeast extract, 10 g. sucrose, 10 g. agar, and 10 ml. 10% peptone solution. The cultures were incubated at 28° C. for 72 hours. The growth was measured by the increase in weight of the culture.

REPORTS

Special Granulomatous Diseases: by Szigeti, H. Jellinek
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On the basis of several cases investigated in detail the following observations have been made:

(i) During infancy and early childhood extragranulomatous lesions occur which represent a transitory form between acute reticulosis of the Letterer-Siwe type and typical granulomatosis.

(ii) In contrast with Letterer's acute reticulosis these forms do not become chronic, and merge into granulomatosis. They differ also from lipid granulomatosis in that they show little tendency to necrosis whereas they readily undergo ulceration.

(iii) The eosinophilic granuloma of bones shows a benign course in about one-half of the cases only. As also shown by a few literary data at most, it may become chronic, and thus partake of a "generalized granulomatous process".

(iv) Lipid accumulation was inconsiderable in the cases described. This fact supports the view that in lipid granulomatosis the storage of lipoids is a secondary, rather than a primary phenomenon.

(v) Between acute reactive reticulosis and lipid granulomatosis there are several transitional patterns. One of these is "generalized eosinophilic granuloma". These processes belong to the same nosologic group. The form of appearance is obviously determined by the age of the patient, considering that acute reticulosis is an infant's disease, transitory forms occur chiefly in early childhood, whereas typical lipid granulomatosis appears in the adolescent or still later. The difference may be due to the fact that the reaction type of the cellular and endothelial system varies with age. Of course, changes of other organ or the reaction of the nervous and endocrinological system and differences in the aetiological agent may be much equally responsible. As to the latter occurrence, very few data are available.

The Problem of the so-called Myocytes: E. Tach, Inst. of Pathological Anatomy of Budapest University Medical School

While studying the granulation tissue formed in the myocardium, Appel and Anitschkov had found, in 1910 and 1913, respectively, peculiar cells characterized by a special arrangement of the nuclear chromatin, this having been collected into the axis of the nucleus. On the nuclear margin of these cells there are projections from which fine filaments start. The filaments run toward the nuclear membrane and it seems as if the entire chromatin mass would be fastened to the membrane by them. These cells had been termed myocytes by Anitschkov and the term has been generally accepted. Many workers have been engaged with studying the genesis and significance of the myocytes. The problem is however still unsettled.

In order to examine the question, the present author examined 100 hearts in which changes due to rheumatic pericarditis were present. In addition hearts from cases of pericarditis, more or less severe, coronary thrombosis, endocarditis and myocarditis with extension and subsequent bacterial endocarditis, were examined; further also injured stabbed hearts, and the operated hearts of three dogs. The hearts of patients who had died of extracardiac disease, such as sudden death during operation of a heart tumor, postoperative deaths, influenza, pneumonia, were used as controls. Beside the myocardium, early and chronic pleuritis, and certain sections of embryos were studied.

According to the examinations, the so-called myocytes are markedly present in the myocardium during the intrauterine and the postmenstrual life. Their number does, however, increase after various lesions following the lesion the cells of the connective tissue of the myocardium, endothelial and perithelial cells, and the cells of the myocardium exhibit a nuclear structure resembling that of myocytes. In none of the extracardiac tissues was the typical myocyte structure found. The topographic and functional conditions of the myocardium apparently favour the development of myocytes. As the peculiar arrangement of chromatin appears in all heart elements after injuries of the heart, especially rheumatism, its genesis may bear some relation to the common mesenchymal origin of these elements. A study of the rheumatic process has shown that this disease exerts a markedly deleterious effect on the myocardium. In the most damaged parts large masses of myocytes ranging in size from 10 to 100 μ diameter can be seen. It is endeavoured to repeat Studnicka's experiments on muscle regeneration and to study in animals the cells and cellular changes occurring in the course of muscle regeneration.

CLINICAL STUDIES OF COLLAGEN IN CONNECTIVE AND ADIPOSE TISSUE

Polarization Microscopy of Collagen Fibres: D. Szabo, I. Banga (1st Dept. of Pathological Anatomy and Exp. Cancer Res. of Budapest University Medical School)

The method devised by Banga for studying connective tissue fibres with the polarization microscope was applied to the examination of collagen fibres. The method is based on the fact that in the native state collagen fibres are resistant to elastase but after heat contraction they become dissolved by elastase ten times quicker than elastic fibres do. Thus, the amount and structure of both collagen and elastic fibres can be measured simultaneously in the same connective tissue.

In the present study the polarization pattern of, and the changes produced by heat contraction and elastase in the collagen fibres isolated from the rat tail were examined.

Elastase brought about swelling of the muscle fibres and the development of a loose

system. At this stage no solution occurred.

When after a pretreatment at 60° to 70° C. the fibres had contracted, the action of elastase results first in their brush-like dissolution (microscopic structure), and then in complete dissolution with a gradual disappearance of the double refraction. The rapidity of solution depends on the duration of the heat treatment.

Subsequently the effect of phenol and the combined effect of phenol and elastase were examined. After treatment with phenol the otherwise synthetic fibres became elastic-like rubber. If phenol and elastase were applied together the fibres became dissolved but rubbery. In contrast with the above case, back to normal state which gradually becomes fibrous with the progress of solution. Their double refraction did, however, not disappear.

The experiments show that the action of elastase yields first in a dissolution of the collagen fibre until to elastic fibres, probably because the elastin causing the fibres to adhere to each other becomes dissolved. Then these fibres develop into granular nests showing no double refraction. If phenol is employed the combination of substances is different.

Pathologic Consideration of the Collagen of the Bone: B. Glusker, J. Gold, S. Mould (1st Dept. of Pathological Anatomy and Exp. Cancer Res. Budapest University Medical School)

Cross and longitudinal examination of the bone of 500 patients was performed. The subjects had been of different age and had died with different diseases. The pathologic conditions displayed by the collagen fibres of the bone tissue is diverse. The first was characterized by the appearance of fat, either as fat tissue replacing the collagen fibres, or as diffuse deposition of adipose tissue in sheets or cells loaded with fat globules observed in the bone. An increased appearance of these cells results in the picture termed "osteitis paraboneal". The cause of these cells results in a variety of mechanisms of normal metabolism. In the second instance of these cells is a result of the mechanism of normal metabolism. In one of our cases the ordinary tissue of the bone proliferation and multiplication of fat tissue. In a female subject the enlargement of the bone secondary to the multiplication of fat tissue. In another case the bone had resulted in removal of one part of the bone.

The second type of changes in the bone tissue is the change of the bone tissue, which can be easily distinguished from the first.

This change may be characterized by the presence of collagenous tissue, which is deposited around the bone tissue.

The third type of changes in the bone tissue is the loss of the deposition and synthesis of collagen, which is a result of the absence of normal metabolism of the bone tissue.

Microscopic Examination of Connective Tissue: G. Szabo, I. Banga (Chairman of the Department of Pathology and Exp. Cancer Research, and Examinations of the Department of Pathology and Exp. Cancer Research, 1st Dept. of Pathological Anatomy and Exp. Cancer Res. Budapest University Medical School)

The changes of tissue may be demonstrated in the fibre system of the connective tissue. As a result of the changes the number, thickness and quality of these fibres are altered. A. The changes may be observed in the number and quality of the connective tissue, which are the result of normal function and pathology of the connective tissue.

B. The changes may be observed in the microscopic structure of connective tissue, which is the result of normal function and pathology.

C. The changes may be observed in the number, thickness and quality of muscle, by means of their number, size, and length, proportion.

the first time, the author has been able to measure the influence of the substrate upon the assimilation of both carbon dioxide and water vapor by a plant.

... they have among the
members much more of freedom
than the members of the other
parties. The members of the
other parties are bound by
the party discipline.

10 *the* *same* *time* *as* *the* *other* *two* *days* *had* *been* *spent* *in* *the* *city*

...and the other two have provided me with

The structure of the dense connective tissue was also more organized showing a more regular arrangement of the collagenous fibers. The more organized arrangement of the collagenous fibers was observed in the connective tissue fibers of the loose connective tissue of the mouth and the skin. The arrangement of the collagenous fibers was more organized in the loose connective tissue of the mouth and the skin.

attempt to observe the double minima usually considered homogeneous. However, the homogeneity of the considered vessels contains important flaws; concerning the homogeneity condition of the diameter of the considered vessel, one can notice that the diameter of the considered vessel is constant only at longitudinal places, while at transversal places it is not constant, as the vessel has a conical shape.

the same time, the number of people who have been infected by the disease has increased to a greater extent. Therefore, during the last year, the number of new cases has increased, and the number of people who have been infected by the disease has increased to a greater extent.

Journal of the Geological Society, Vol. 100, A. Long, Geol. of Argyllshire, p. 100.

The nature of the culture differs from the nature of the trophic phases, the first and last, the second and the more numerous intermediate. The differentiated by means of Dosty's method, which distinguishes precisely.

The spaces are not only run between the collagen fibres but also interminate them. As to the size of such spaces, the collagen fibres are surrounded by a plasma formed by one or more myofibrillar filaments. From the plasma, fibres enter into the substance of the collagen fibre, as demonstrated on cross sections. On cross sections stained according to von Gieson or with other methods it may be seen that the substance of the collagen fibre is not homogeneous, there being granular areas to be distinguished within the otherwise uniform cortical zone. Attention is called to some recent data on the so-called ultra-structure of the collagen fibres. In the view of many authors, such as Bergmann, the ultra-structure would be in relation with the fluid metabolism (swelling and shrinking) of the collagen fibre. The storage fluid accumulation in the intervertebral disc demonstrated by the present author.

Schäfer-Bücher's terminal reticulum surrounding the nuclei of the collagen fibres are demonstrated. The authors agree with Schäfer-Bücher that these reticula cannot be demonstrated except in perfectly unprepared specimens, and that their examination requires much skill and experience. The pictures demonstrated have been taken with the aid of Abbé's apparatus.

In the cricoarytenoid ligament a ganglion consisting of multipolar cells was found. The processes of these cells are in continuous connection. The cell bodies lie on the collagen fibres.

Among the nerves running to the collagen fibre tissue and thinner fibres may be distinguished. The authors believe that the plies of the collagen fibres contain both efferent and afferent pathways, and the thickness of the fibres may, as in the case of spinal nerves, represent qualitative differences. These examinations may help to extend the field of nervous. The results confirm those of T. A. Grigoryeva (1953) who has observed, after extirpating the sensory nerves of various organs, a distinct reaction of the connective tissue, manifesting itself in a destructive infiltration accompanied by loss of the organ.

Innervation of the Connective Tissue. A. Andrianov (Inst. and Inst. Institute of University, Saratov)

The nerve supply of the connective tissue always depends on its size and function. According to this, the innervation may be rich or poor and the connective tissue may contain various vegetative cells, fibres, plexus and an immense quantity of end apparatus. Beside them, as seen in sections made from the spleen capsule, omentum, cornea, endocardium, peritoneum, and the swimming bladder, impregnated according to Rieberowsky Gross, and Melchiorovsky Abrikosov, the elements of the connective tissue also have their own innervation. This cannot be demonstrated except in certain areas and in relation to cells only. In the structureless intercellular spaces only delicate plexuses and a meshwork bearing no terminal apparatus can be seen. Data as to the innervation of elastic fibres are still lacking, for technical reasons the problem cannot yet be solved. The rich contacts of the fibres suffice, however, for the physiological demands. In contradistinction to this, it is certain that nerve fibres run along the collagen fibres in the wall of cerebral vessels and, in some instances, even nerve terminations forming thin, elongated plexus could be demonstrated on the collagen fibres. It should, however, be emphasized that terminations of this kind are, like in other vessels and in the swimming bladder, pressureceptor endings of other origin rather than the own terminations of the connective tissue. The existence of the own innervation of the connective tissue cells be proved in the lamina propria of the cornea. The fine varicose fibres pass through several cells with which they form a physiological unit, to terminate on the last cell of the eventually branching plexus.

Constitutive Data to the Significance of the Interstitium of Peripheral Nerves. M. Wahr, P. Bláthich (Dept. of Histology and Embryology of Budapest University Medical School)

The route of vital dye injected into peripheral nerves was observed. 130 rats were used in the experiments. Indian ink and lithium carbon were injected into a nerve, its environment, and the subarachnoidal space. The material was worked up 2 hours to 120 days later.

The experiments have shown that no dye passes from the environment into the nerve through an intact epineurium. The dye gets into the nerve only through an injury of the epineurium and becomes partly phagocytized by the white blood cells abundantly immigrating after the injection. Subsequently the leucocytes disintegrate and their constituents, together with the dye, are taken up by macrophages which follow the leucocytes. If a suitable amount of dye had been administered, phagocytosis was started after 48 hours by the Schwann cells, in the cytoplasm of which the dye appears in the form of fine granules filling the cell incompletely. This process lasts for about 72 hours. Then the macrophages become more and more round, more and more dye accumulates in their cytoplasm, they take place within gradually decreasing groups lodged in larger and larger connective tissue bundles until, by the 120th day, no dye is found except in the epineurial cells of the fibrocyte type. The nerve itself becomes entirely free of dye.

The chief point of the results is the fact that some light has been thrown upon the protective function of the interstitium of the peripheral nerve. It has been shown in which way the interstitium reacts to the entry of a non-living foreign substance of colloidal size, which of the components take part in the reaction and how long the process lasts. Out of the participating elements

the Schwann cells of ectodermal origin should be pointed out, since up to now their transformation to macrophages and their ability of phagocytizing dyes could be demonstrated only in tissue cultures. Their transformation to macrophages in vivo will form the subject of further studies.

Nerve-sympathetic Regulation of the Reticuloendothelial System of the Liver:
Gy. Csiba, Gy. Rappay, B. Niedermann (Dept. of Histology and Embryology of Budapest University Medical School)

The storing capacity of the hepatic reticuloendothelial system was studied in white rats by means of Tiss and Valley's method consisting in the microchemical estimation of silver which had been administered *in vivo*. In earlier experiments the regulating effect of the nervous system on the capacity of storing had been examined. In those experiments the storing function of the hepatic reticuloendothelial system had been enhanced by stimulation of the substantia nigra sympathetic centre whilst parasympathetic stimulation had exerted a depressing action. A similar depressive action had been effectuated by the cortex, especially the frontal lobe, through inhibition of the substantia nigra sympathetic centre.

The question arose whether this was a direct effect or an indirect one produced by hormones. Therefore we examined the effect of insulin, adrenalin and the adrenal cortical hormone, further this relation to nervous regulation.

Insulin exerted a decreasing effect on storing; 1 unit per 100 g body weight lowered the storing by about 25 per cent. No effect of a similar intensity had been observed to be brought about by the nervous system. The effect could be strengthened by increasing the dose: administration of 5 to 15 units resulted in a decrease of 45.5 or 72.5 per cent, respectively. No correlation was found between the blood sugar level and the storing capacity. It could be demonstrated by administering benzedrine or with lobectomy that the insulin effect decreasing the storing capacity was produced through the frontal cortex.

The effect of adrenalin on storage was incommeasurable unless enormous doses were applied. On the other hand, adrenalectomy resulted in a 72.6 per cent decrease in storage. The decrease could be compensated by administering adrenal cortical extract while adrenalin in normal doses was inefficient. The stimulating effect of the central nervous system becomes lost after adrenalectomy.

On the Ultrachemistry of Gaucher Cells: A. Szűcs, B. Maróthy, K. Kovács (Dept. of Pathological Anatomy of the University Medical School, Szeged)

The reserved option of a female child suffering from Gaucher's disease was examined by histochemical methods.

The cytoplasm of Gaucher cells stained red with hematoxylin and eosin, brown with von Gieson's stain, bluish red with Giemsa's stain. No elective staining was observed with Giemsa's chromate-alum-haematoxylin method. Toluidine blue and methyl violet stains did not result in metachromasia. Neither sudanophilia (Fischer III) nor argyrophilia (Gomori) was observed. Thymonucleic acid (Perry's test) and birefringent lipid substances (using a polarization microscope) could not be demonstrated either. Lorain-South and Bielschowsky staining method led to a negative result whilst Feijer's haemalum method resulted in a positive colouring. On Mallory's trichrome stain the cytoplasm showed acidophilia (blue), and Schiff's periodic acid a markedly positive reaction was obtained. Previous boiling in chloroform-methanol had no influence on the staining reactions. On treatment with methyl green, the cytoplasm exhibited an intense pyroninophilia which did not occur if the material had been treated with hydrochloric acid. This fact was indicative of the presence of ribonucleic acids. Following extraction with pyridine, both acidophilia and the positivity of the periodic acid-Schiff test disappeared whereas pyroninophilia remained unchanged.

In the opinion of the authors, the essential feature of Gaucher's disease is by no means a passive intracellular storage of transportable carbohydrates; the disease should be regarded as a systemic affection of the reticuloendothelial system in which an enzymatic deficiency of the reticular cell system is followed by intracellular production and accumulation of lipop-

Experimental Reticulosis: A. Szűcs, B. Maróthy (Dept. of Pathological Anatomy of the University Medical School, Szeged)

In the course of investigations on the antineoplastic action of tannic acid the efficacy of unpurified preparations was also studied. The aqueous solution of one of these substances (Valex) was administered to white rats in gradually increasing doses for prolonged periods. The treatment was well tolerated, the majority of the rats survived the 300th day. The gross histological

... observed in previous experiments hardly seemed to these authors. On the other hand, histology of their bone marrow, spleen, and lymph nodes revealed nothing changes. Maturation and proliferation of reticular elements were not observed. The normal conditions of lymph nodes had been probably replaced by plasma cells, histiocytes and endothelial cells, mostly with the predominance of one of these types. The normal structure was mostly destroyed, although the predilection of plasma cells was more than one of a degree from a malignant process.

Profound changes occurred in the spleen as well. As a rule, proliferation of megakaryocytes proceeded, but histiocytes and plasma cells, which were present in noncancerous lymph nodes were also seen. The last authors were hypothesized:

"It seems that chronic proliferative changes in lymph nodes could be not very much in accordance with the primary tumor, but, only a diffuse proliferation of lymph nodes, the reticular tissue, the lymphoid tissue, and the lymphoid vessels in accordance to the number of lymph nodes, the spleen and the lymphatic vessels is necessary as to removal of the part of the mass, the diagnosis of cancer is made."

A further study of the question of the origin of the noncancerous changes may need new facts concerning the pathogenesis and the mechanism of reticuloendothelial system, so they may come the satisfying answer.

The Lymph System of the Stomach and its Behavior in Gastric Ulcers Sergej Vojnov and Gy. Balony (Department of Urology and 2nd Dept. of Pathological Anatomy of Budapest University Medical School)

In the surroundings of gastric ulcer the lymph nodes of all layers of the stomach become enlarged and thus it is possible to study their topography. A detailed description of the vascular and lymph ducts is given, including their number and location. It is emphasized that the number of lymph vessels revealed by this procedure is considerably less than the number found with the histological method.

The dimension of the lymphatic system is correlated to the dynamic status of lymph vessels.

The question is raised whether postoperative adhesions, i. e. constrictions of the bowel to a certain area might not be due to a tumor of lymph ducts.

Congenital Abdominal Hernia and its Surgery I. E. Szilagyi, B. Szilagyi (1st Dept. of Pathological Anatomy and Surg. Cancer Unit of Budapest University Medical School)

Morbidities in 1947 was the first of Szilagyi congenital abdominal dysplasia, a condition characterized by a hyperactive mesothelium within which a free bowel are only present. In 1948, only a thickening of the abdominal septa occurs, with a decrease of the suspensory ligaments.

In 1950, Szilagyi and Ostor examining the lungs of 37 newborn infants found one case of congenital abdominal dysplasia in 28, i.e. 3.6 per cent.

We have examined, in the years from 1948 to 1952, the lungs of 135 infants who died in the first week of their life. 30 of the infants had been mature, weighing 2000 g, or less, average 1720 g. All in all, 11 infants, i. e. 36.7 per cent, displayed congenital dysplasia, the degree of which was severe in 3 (3.4 per cent), moderate in 5 (5.4 per cent), and mild in 3 (3.4 per cent) cases.

In the severe and moderately grave cases the lung contained of a hyperactive mesothelium in which very few vessels were present. In mild cases thickening of the interstitium occurs.

Establishing the respiratory failure, congenital abdominal dysplasia is a serious, but not so common liability. 31 per cent of our positive cases had died within 24 hours after delivery, so it may be inferred that it is in the first hours and days that life is endangered by the condition.

The combination of congenital abdominal dysplasia with other developmental anomalies is not more frequent than its occurrence by itself. That is, however, one exception, viz. central diaphragmatic hernia. The latter condition occurred in 4 of the cases examined, and in all four a grave abdominal dysplasia was present on the side of the hernia while on the other side the change was considerably milder. It seems therefore possible that mechanical factors may play some role in the development of the condition. In our opinion congenital abdominal dysplasia represents a developmental anomaly, more precisely a condition due to a delay in embryonic development.

Section of Early Identification and Comprehensive Rehabilitation opened **October 20, 1970** at **University of Pennsylvania Medical Center**

After applying 600 to 8000 μ to the whole body or 1000 to 2000 μ locally in either case, the most cells of the epidermis undergo degeneration and of the secondary cellular components, degeneration of the connective tissue, the basal layer of the epidermis and their desquamation, occurs after four hours only. The basal desquamation is generally followed within 24 hours by regeneration of the secondary cellular components in the basal layer. When applied to the skin, the epidermal cells undergo degeneration and regeneration of injured cells is stimulated by the action of the secondary cellular components held surrounding the basal cells covering the epidermal area and there is less skin loss than the chemical irritants.

The secondary cellular components can be produced by 1000 to 2000 μ of 10^{-3} Molar concentration of 10^{-3} Molar $HgCl_2$ for 10 min. After being washed off, the secondary cellular components are obtained.

It is observed that the growth in the epidermal system, however the degree of growth is not as good as the control group in the respect.

University of Michigan Committee on the International Conference on Chemistry.

Standardization of Wound Dressing by Autoclave **and**
Autoclaving Standard Dressings **in** **Sterile** **Wounds** **by** **A. A. Azev** **(Dept.** **of** **Microbiology** **and** **Parasitology,**
of **Tunisian** **University,** **Tunisia)**

The origin of this industry was started by men both married and wedded with women, who worked closely in their trade. On the first day married down, continuing months and years, until he or woman were. This is an industry

decreased. By the beginning of the week the new granulation tissue is a looser mesh of fibers with an irregular mesh. The number of nuclei per unit area of granulation tissue is increased with increasing time. The density is more increased and a more dense granulation tissue also forms. In other words, granulation tissue is more developed and more densely packed. It is observed that the granulation tissue is more developed and contains many more nuclei than in this experiment. These points may have some role in the regulation of the growth of the granulation tissue. As the granulation tissue grows, the density of nuclei in the granulation tissue may also be increased. In certain conditions, however, the density of granulation tissue is more reduced.

Application of the Tissue Grafting Procedure Method of Hydrocortisone Formation of Anatomical Nodules During the Immature Stage (Dr. J. S. D. and Department of Surgery and 2nd Dept. of Pathological Anatomy of Dhaka University Medical School)

The problem was raised how an anastomosis could be brought about between the vessels of the alimentary tract without exposing the lumen. We have attempted to bring about anastomosis between the stomach and the rectum either between the mucous membranes or between the serous membranes. First the rectum where anastomosis was to be created was cut open and the rectal wall was stripped of its mucous membrane. Then hydrocortisone gel was applied to the border, the area treated by hydrocortisone gel was held upon each side and bathed with warm water. The application of hydrocortisone gel resulted in removal of the rectal mucous of the rectal lumen has removed through the rectal lumen. After hydrocortisone was prepared in form, just as follows in 4 days. All anatomical structures were intact. Gross and microscopic preparations are presented.

Cytologic Observations in Healing Wounds by H. H. Hildebrand & Dr. S. S. Devadoss, Dept. of Pathological Anatomy of Dhaka University Medical School

In healing skin wounds of rats a thick fibrillar network is found within the wound during the first 24 hours. In the intercellular spaces, lymphocytes and eosinophils are frequently present. The cytoplasm of macrophages contains frequently vesicles. The nucleus is usually large and located near the nucleus which becomes eccentric and forced to the side. In other macrophages the cytoplasm contains a dense substance which stains dark red with methylene blue and which changes gradually with the other parts. In others with the cytoplasm remains pale pink, stains dark violet or blue, and have a shiny surface surrounded by a vesicular-like border. At this stage the globules stain intensely with nuclear dyes. The original nucleus is usually forced to the side and surrounds the globule at the time of a convulsion. The appearance of the features of a nucleus occurs gradually near to the cell border and in this way the structure of the nucleus of the mother cell is preserved during this process. Some of the nuclear globules are small, while others are surrounded by a thin, pale, circular cytoplasm.

Although the further development of nuclear convulsions could not be observed in the studies, it is believed that a process of cell division begins two weeks later. It seems probable that the diffuse nuclear substance of the cytoplasm condenses into a rounded nucleus which later becomes expelled from the cell. The main feature of the phenomenon observed in the nucleocytoplasma observed by Paul Ehrlich is not possible to observe due to the difficulty in histological sections. The authors wish to study the problem in tissue cultures.

Evaluation of Connective Tissue and Nerve Fibers in Healing Wounds Dr. S. S. Devadoss, L. Hildebrand (Dept. of Pathological Anatomy of Dhaka University Medical School)

Studies were made to observe the healing of skin wounds in rats, with special regard to morphological changes and their chronological sequence. The results will serve to supplement the quantitative test previously reported. The wounds were examined in several series. In the first two days, tissue samples were taken every 4 hours, then once daily until the 10th day. Small sections of the nerves were examined by Cajal's black impregnation method modified by Troxley.

The following chronological sequence was observed in the morphological changes. (i) On the 1st day perivascular foci of granulation tissue appear in which an intercellular metachromatic and horizontally arranged argyrophilic fibers are present. (ii) On the 5th to 6th day cavity is filled with granulation tissue containing a horizontal argyrophilic fiber which becomes metachromatic reaches its peak and the number of lymphocytic histiocytes is lowest.

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SOME ASPECTS OF APPENDAGEAL WOUND HEALING AND REGENERATION.

(ii) On the 7th day a vertical vascularization is seen in the granulation tissue. (iv) On the 10th day the granulation tissue shows signs of aging, i.e. collagenization and a somewhat decrease of cells and vessels.

The fibre system of the granulation tissue invariably seems to develop from the extra-cellular basic substance lying between the fibroblasts. The fibre system deriving from the fibroblasts was inaccessible to observation.

In contrast with literary data, innervation of the granulation tissue was found to develop parallel with the development of the tissue itself. Nerves appeared from the 5th to the 10th day. According to the site of their origin, the following groups of nerve elements could be distinguished. (i) Nerves starting from the wound edges. (ii) those originating from the intact tissue of the wound base. (iii) nerves originating from proliferations resembling angiogenesis appearing in the area where the muscle had been severed, nerves accompanying the vessels of the granulation tissue.

Bleeding after Repeated Skin Injuries: Gy. Györy (Dept. of Pathological Anatomy of Budapest University Medical School)

If on the back of white rats a second skin wound measuring 1 square centimeter is repeatedly caused, the course of healing exhibits considerable morphological and quantitative changes. With the increase of the number of successive healing takes more and more time. In the vessels and fibres of the granulation tissue a high degree of hyalinosis occurs which is never seen in a primary wound. The hyalinous membranes shield the capillaries with a hyalinous thickening of the basal membrane, or the small arteries with hyalinization of the media and adventitia, constricting the lumen. After healing a nearly avascular thick hyalinous mass is found on the basis of the wound. The hyalinous basic tissue represents changed conditions for the new injury. The vessel changes observed in such cases resemble those found in chronic processes of different aetiology. The changes are presumably due to destruction of the basic tissue produced by the injury, rather than to repetition or chronicity of the damage. The statement, according to which a second wound heals more quickly than a first one, has not been confirmed by the observations, but it may be valid if the second injury occurred before the primary wound had healed; in this case, protein catalysts may be absorbed from the wound not yet healed.

The so-called Amyloid Tumour of the Larynx: L. Molnár (1st Dept. of Pathological Anatomy and Exp. Cancer Res. of Budapest University Medical School)

The histologic picture of amyloid tumours was studied on 30 biopsy specimens. The experiments have shown that in their development three stages can be distinguished. Initially, the epithelium is intact or compressed, the subepithelial tissue is oedematous, it contains dilated blood and lymph capillaries, and stains as in mucoid degeneration. Later, the vessels running in the oedematous and mucoid tissue become surrounded by a homogeneous mass invading their adventitial and medial layers. Though the mass does not stain uniformly, it characteristically gives a positive reaction to Weigert's fibrin stain and exhibits no metachromasia. In the terminal stage the mass becomes more consistent and forms a network and bundles of a concentrical, parallel or branching arrangement. The vessel wall becomes thicker and homogeneous. At the same time the process extending from the vessels toward the periphery. In consequence of this the lumina of the vessels may, in later stages, undergo compression. At this time the tumour is rather large and its histochemical structure is changed. It turns orange with copper-red, yellow with van Gieson's stain, dark blue with Mallory's method and does not react to Weigert's fibrin stain, its name, eosin, gentian violet and iodine green, may result in metachromasia, especially in the centre of older foci.

As mentioned above, these phases can be distinguished in the development of amyloid tumours, via. mucous oedema, fibrin precipitation, and secondary changes. The latter results as a rule in a hyaline-like mass whilst a histological structure resembling amyloid is less frequent. Aside from the fact that these tumours have no relation to general amyloidosis the term amyloid is inappropriate on the basis of both their histology and histochemistry. The term "fibrillar hyaline tumours suggested by Röthke-Hermann seems to be more correct."

Connective Tissue and Amyloid: A. Szilagi, L. Grosszky, L. Bánk (State Military Hospital, Budapest)

In numerous breast and skin cancers, parotid tumours, adenocarcinomas of the intestine, pulmonary cancer, etc. the authors have found a substance staining red with eosin and yellowish brown with van Gieson's dye. It reacted invertibly with a bright brown-red hue to Congo.

ELASTIC SUBSTANCES IN TUMOURS AND OTHER TISSUES

With to methyl violet, polychrome methylene blue and toluidine blue its reaction was varying, sometimes the substance stained like amyloid. The variety of the reactions may be due to the age of the precipitate. Its most mature form is amorphous-granular. This appears e.g. in breast cancer around vessels and ducts, or between cancer cells. In other cases it is situated in strands in the form of broad plates lying around skin tumours in the corpus papillatum. In the evolvement of the homogeneous to finely granular masses, earlier phases of precipitation may be found in the form of twisted or wavy, often broken fibres and filaments, frequently constituting a dense meshwork between the cancer cells. Both the filaments and the granular masses give rise to elastic stains. After treatment with elastase this reaction fails to occur and no does the congo red reaction. Neither the organs of subjects with secondary amyloidosis, nor their amyloid masses (skin, liver, larynx) react to elastofluorin nor are they accessible to elastase. There is still another histological difference to the well-known amyloid, since tumour amyloid fails to stain diaphoretically with congo red while normal and basal amyloid substances display marked double refraction after staining with that dye. Another difference appears on the application of osm. after which the normal amyloid appears blue similarly to the matured amyloid, but younger forms give a yellow, orange, or red colour. Therefore, the term elastic amyloids has been suggested.

The initial stages of the process were examined in animal experiments in which immunized plasma decomposition was produced by X-ray irradiation of transplanted tumours. The amyloid diffuses at first the elastic elements of the vascular wall. Later on, amyloid masses independent of the vessels may be seen. The occurrence of amyloid in tumours and their surroundings is thought to result from an antigen-antibody reaction; the antigen would be furnished by the cancer elements whilst the antibodies might be formed either in the tumour itself or in remote organs. If a mixture of antigen and antibody is injected intradermally to animals, a congophilic substance becomes soon formed in the swollen area. The adsorption of paraproteins reacting with amyloid is frequently preceded by the increase of elastic elements. Finally, the role of plasma cells is discussed. On the basis of the observations and literary data it is believed that the occurrence in malignant tumours of the nonspecific substance termed elastic amyloid might be a product of an antigen-antibody reaction which should, in the view of the author, be linked with the other defensive phenomena of the organism affected by cancer.

Cultivation of Granulated Tissues I. Palyi (Dept. of Histology and Embryology of Budapest University Medical School)

Cultures were made from foreign body granulation tissue. The experimental animals were rats. The age of the granulation tissue to be cultivated varied from 1 to 30 days. The tissues were cultivated on Maximov's medium for from 1 to 21 days. In the young cultures of granulation tissue (1 to 6 days) the multipotent macrophage cells appear first, then fibroblasts, fibrocytes, and many irritation forms follow. From the capillaries of the mother culture endothelial cells grow out. In middle-aged cultures (7 to 15 days) giant cells present themselves and elastogenesis appears. In old cultures (15 to 30 days) a slow fibroblastic growth may be seen. The epithelialized growth of connective tissue cells is a characteristic feature. This epithelialized tissue becomes on the 12th day disintegrated into fibroblasts presenting no sign of degeneration. In cultures of old granulation tissue displaying an epithelial growth the degenerative phenomena developing with the progress of cultivation time appear much later than in cultures of a similar age, prepared from young tissue. Granulation tissue cultures possess a very strong growing tendency, shown by the short latency after explantation. The connective tissue of grown up rats which served as control displays a very slow or no growth whereas the growth of the granulation tissue started intensely after a latency of 12 hours.

Development of Elastic Elements in Tissue Cultures: Gy. Lelkes, B. Soma (Dept. of Anatomy of Debrecen University Medical School)

The behaviour of elastic elements, further the appearance of newly formed ones, was examined in cultures of embryonal chicken's heart and aorta. In pulsating heart cultures, taken from chicken embryo three to seven days old was cultivated by Maximov's method on a medium containing equal amounts of chicken plasma, Tyrode solution and chicken embryonic fluid. Occurrence of elastic fibres was observed in the proliferation zone. No correlation was found between the duration of pulsation and the quantity of elastic material. In cultures displaying pulsation after explantation no elastic elements were produced. Similarly elastic elements failed to be formed if the nutritive medium had been prepared without chicken embryonic fluid.

although in these cases pulsation lasting for several weeks was attained in addition to slight proliferation.

No formation of elastic fibers occurred in necta cultures. The elastic fibers of the necta culture underwent granular decomposition. If the necta is cultivated in a way that its competition with a pulsating heart culture is preserved, the elastic elements remain unchanged and signs of new formation may even appear.

Newly formed elastic elements occurred in the presence of cells only. In the authors' opinion, elastic elements develop in connection with mesenchymal cells, which form elastic fibers according to environmental conditions, either by a formative or by a fermentative function.

In the view of the authors, pulsation is not the only factor in the formation of elastic elements. It may, under the experimental conditions given, play the role of an exciting agent. On the basis of the observations made on necta cultures, pulsation should be considered an adequate stimulus of the preservation of elastic fibers.

Formation of Elastic Elements under Embryonal, Postembryonal, Regenerative, Pathological and Explantation Conditions. I. Krasznayka (Dept. of Anatomy of Debrecen University Medical School)

The prerequisites of the successful examination of elastic fiber formation are (i) fresh material, (ii) in which elastic elements are being formed at the time and place given, (iii) adequate macroscopic preparation. Deteriorated material, or any finally prepared substance or a substance in which elastic fiber formation does not take place at the time of the examination cannot be evaluated. In material prepared by itself or reported in the literature, provided that the substance corresponded to the requirements mentioned above, the author invariably found light cells of mesenchymal origin. These cells are demonstrated on 15 microphotographs. The elastic elements appear on the surface of these cells as a fine, cerebriform membrane. The author never observed formation of elastic elements if these cells had not been present. The formation or deposition of elastic fibers was never observed in epithelial or brain tissue. Since formation of elastic elements is, under embryonal, postembryonal, regenerative, pathological and explantation conditions always accompanied by the presence of these cells, some role, either formative or fermentative, must be attributed to them in the formation of elastic elements, wherever they should be termed elastoblasts. It would be erroneous to consider the elastoblasts as cells determined *a priori*. They obviously originate from the ubiquitous mesenchyme or the postembryonal mesenchyme derivatives under the effect of local functional factors i. e., the intermittent traction results in their differentiation. The formation of elastic fibers is influenced also by the hormones, vitamins and enzymes of the original organism; they are dispersed in the tissue fluids at the site of elastic fiber formation. If they are missing, the formation of elastic elements does not occur, as seen from the experiments of Leches and Karmanoff who have failed to obtain elastic fibers if embryonal extract was not added to the tissue culture. Thus, the absence of a single factor may inhibit the formation of elastic elements e. g., dried material cannot be produced under inflammatory conditions.

Elastic material was never produced in the absence of cells. Its formation without cells has been repeatedly assumed. This remains, however, a mere assumption until the material will have been demonstrated on material answering the requirements mentioned.

Changes in the Structure of the Adrenal Cortex in so-called Collagen Diseases E. Farben, L. Pethreyes (1st Faculty Hospital, Budapest)

The changes accompanying the function of organs may perhaps best be seen in the striated muscle in the endocrine organs, e. g. in the pituitary gland, the ovary and adrenals. The changes are neither uniform, nor specific. The complex function attributed to the pituitary gland is accompanied by a more variable histochemical pattern whilst the morphological and histochemical structural changes of the adrenals display less variety, their functional spectrum being comparatively simple. Although the morphology of the adrenals has been studied for nearly 100 years, the results obtained are strikingly poor. The uncertainty manifested mainly in the evaluation of adrenal function, i.e. in establishing the zonational and functional differentiation of the halo, gluco- and androsteroids, appears also in respect to morphology. The division of the cortex in three layers on a pure morphological basis is less real than a functional differentiation in the sense of which an outer, or regenerative (dissociated), a middle, or functional,

In comparison of the elastic fibres the otherwise rigid flat wavy collagen fibres are distended with the former ones. The failure of heat contraction of the too hot fragment may be due to the fact that the substance binding collagen fibres to elastic ones is at the same time responsible for heat contraction.

Collagen fibres of elastic arteries behave like those of the aural ligament; their structural-chemical relationships are probably also identical. Silver impregnation and sulfurous staining application of elastolytic and heat contraction, make it possible to demonstrate the elastic tissue and collagen, and their increase or disappearance in various pathological conditions.

The Role of Lipids in the Elastolytic Dissolution of Sclerotic Arteries László, B. Schindler (1st Dept. of Pathological Anatomy and Exp. Cancer Res. of Budapest University Medical School)

The aorta of 24 subjects affected by atherosclerosis of varying severity were examined. For estimating the total cholesterol and phosphatidol content, frozen sections were made of the arteries. The sections were placed into a solution containing 2 mg per ml of Triton and collagen-crystalline elastase and incubated at 37° C for 15 minutes. The extent of lysis was evaluated from the swelling and fragmentation of the elastic elements, and from the decrease in number. The following results were obtained:

1. During the progression of atherosclerosis the cholesterol content of the vascular wall considerably increased, the amount of lipids to a lesser extent.
2. Elastolysis is inhibited by the lipids of the vessel wall. This effect is probably due to the action of lipids on permeability.
3. With the progress of sclerosis the elastolytic solubility of elastic elements increases. This might be due to a structural transformation of the fibres.
4. The ratio cholesterol per protein has no demonstrable influence on the elastolytic dissolving effect of lipids.

A Possible Viral Process of the Pulmonary Elastic System: B. Schindler, L. László (1st Dept. of Pathological Anatomy and Exp. Cancer Res. of Budapest University Medical School)

A child 2 and a half years old developed attacks of increasing severity, occurring both at night at intervals of 10 to 15 days. The attack was accompanied by prostration, tachypnoea, cyanosis, and a temperature rising to 39° C. During the attacks X-ray revealed in the lungs small foci resembling those of miliary tuberculosis. After the attack had lasted 2 to 3 days the foci disappeared. Between the attacks amounts of the regenerative type eliminated the condition. The severest attack caused fataly. No clinical diagnosis could be established. Autopsy revealed a grave brown induration involving nearly the whole lung and enlargement of the peripheral lymph nodes. In the other organs (the heart included) no marked change was found. Microscopic examination revealed dissolution of the elastic elements both the pulmonary capillae and the small vessels, their impregnation with iron, phagocytosis of perivascular giant cells and mastocytes. The connective tissue was thickened, the blood filled erythrocytes and leukocytes. At places perivascular lymphocytic infiltration surrounded fragments of elastic fibres with the perivascular inflammatory reaction elicited by them were present in the regional lymph nodes. The pathological process was found in other organs apart from a few perivascular foci which had been observed in the kidneys and the adrenal glands. In view of the microscopic findings the disease was regarded as a case of eosinophilic granuloma or histiocytosis X. This syndrome had been first reported in 1931 by Greifen. More than 20 cases have been published. The disease process consists in a change of the elastic fibres. The literature contains no data on the etiological factor causing dissolution of the elastic fibres. Since because of the short duration of the attacks the lymphocytic infiltration can occur in all organs simultaneously, pulmonary haemorrhage being a feature of the disease, an allergic origin seems likely. A secondary haemorrhage being a disease of the elastic elements, its role in the course of the disease must be attributed to elastolysis.

Immunotherapy and the Pulmonary Elastic System: J. Juhász, G. Nagy (1st Dept. of Pathological Anatomy and Exp. Cancer Res. of Budapest University Medical School)

The effect of pentavalent avian immunotherapy was examined in white rats. 20 rats were given 0.5 ml of a 10 per cent solution intraperitoneally twice a week. Each ml contained 100,000,000 organisms, corresponding to a total of 0.15 g of organisms.

The Role of Endothelial Plastin in the Mechanism of Dissolution of Sclerotic Arteries

The Role of Lipids in the Fluorocarbon-Induced Myopathy **David B. Laskin, D. Schuler, and D. Pyle** *Department of Pathology and Anatomy, and the Department of Medicine, Mayo Clinic, Rochester, Minnesota 55905*

The results of 23 patients with primary biliary cirrhosis are summarized in Table I. The mean age was 50 years, and the sex ratio was 1 male to 1.5 females. The total cholesterol level was raised in all patients, and the mean serum triglyceride level was significantly increased. The mean serum HDL-cholesterol level was significantly decreased, and the mean serum VLDL-cholesterol level was significantly increased. The mean serum LDL-cholesterol level was significantly decreased. The decrease in

That is, the probability of a false alarm is α , and the probability of a miss is β . The probability of a correct detection is $1 - \beta$.

¹ The author would like to thank the editor and anonymous referees for their useful comments and suggestions.

The exact role of lipids in the structure of the fibres is not known, but it is clear that they exert a considerable influence on the rheological effect of lipids.

A Peculiar Morbid Process of the Endocrine Glands

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A hold (and a half years) was developed by the lack of increasing and the ceasing before than intervals of 10 days. The disease attacks were accompanied by elevation of the body-temperature, loss of appetite and temporary enlargement of the liver. During the disease X-ray revealed a diffuse, non-specific infiltration of the lungs. The disease course of the attack had lasted about 10 days. It followed a considerable time after the first attack. The disease had been of the progressive type, but it did not end in death. No terminal diagnosis could be made. Anterior-posterior and lateral X-ray of the chest involving nearly the whole lung and a portion of the great vessels of the heart. The heart was enlarged, the heart-lung ratio increased to 1.42. Many signs of vascularization, i.e., destruction of the elastic elements in the pulmonary tissue and the spaces between them, congegulation with non-phagocytosis of the cellular debris and the cellular debris. The alveoli wall was thickened, the alveoli full of exudates and cellular debris. The cellular infiltration by neutrophil and lymphocytes occurred in the spaces of the elastic fibers and the spaces between them. The inflammatory reaction, elicited by them, consisted of basic fibers and the spaces between them. The inflammatory reaction elicited by them, consisted of basic fibers and the spaces between them.

Bronchiectasis and the Pulmonary Elastic System. J. Johnson, G. Kendrew
Dept. of Pathological Anatomy and Experimental Tech., St. Bartholomew's Hospital Medical

The effect of protracted methane administration was evaluated in white rats. 20 rats were given 0.5 ml. of a 10 per cent solution intraperitoneally twice a week. Each rat received 0.5 ml. amounting to a total of 1 ml. of methane.

1.0% methane was injected into the trachea of 100 animals.

2 to 16 months after the last injection the animals died in a cachectic state. In 54 of the 100 per cent) bronchiectasis was found. Spontaneous bronchiectasis occurred in 3 of 40 animals (7.5 per cent).

Bronchiectasis may occur in any of the lobes. Most frequently it is a smaller dilatation containing mucus and pus. The destroyed smooth muscles and elastic elements of the bronchial wall have been replaced by hyaline scar tissue. The surrounding lung tissue is fibrotic. In each case the bronchial wall shows severe inflammatory changes. The inflammation destroys the smooth muscle and elastic elements of the bronchi which later dilates. Thus the primary factor in this kind of experimental bronchiectasis is a destruction of the elastic elements of the bronchial wall. The bronchus devoid of elastic elements becomes gradually dilated by its own mucus-laden exudate. The destruction of the surrounding lung tissue constitutes an additional factor in the dilatation. The most severe examples of bronchiectasis were found in animals which died at the end of the experiments.

It is a fact well-known from clinical and experimental observations, that the organism treated with methane becomes susceptible to infection. In the present experiments the decrease of resistance due to methane led to extensive bronchopneumonic inflammation which was further aggravated by the local effect of the urethane excreted in the bronchi. The inflammation resulted in destruction of the elastic system followed by dilatation of the bronchi.

In 2 of the animals (10 per cent) a pulmonary adenoma was found. In the 40 controls no tumour occurred.

Experimental Hypertension and Vascular Necrosis: J. Lechner, Gy. Gárdos (1st Dept. of Pathological Anatomy and Exp. Cancer Res. of Budapest University Medical School)

The aim of the examinations was to study the pathogenesis of acute arteriolonecrosis accompanying malignant hypertension.

By means of an own method malignant renal hypertension was induced in albino rats. Part of the animals were bled to death while still in a good condition, the others directly before their spontaneous death. In all cases the non-protein nitrogen level in the blood was estimated. In some of the rats severe azotemia was found, in others the NPN was nearly or completely normal. Microscopically anemic and non-anemic animals revealed no difference in vascular changes, nor was any correlation found between severity of arterial lesions and degree of azotemia. It was concluded that the toxic factor represented by urethane feeding rather than the development of arterial necrosis.

Killing the animals in different phases of the experiment made it possible to study the histogenesis of arterial necrosis. It could be established that the arteries turns into hyaline in a very short time (1 or 2 weeks).

Comparing the cases of experimental renal hypertension taking into account malignant type the following could be observed:

(i) Neither urethane nor allergic factors play a part in the production of arteriolonecrosis which attends malignant hypertension.

(ii) The main factor in the production of acute arteriolonecrosis is the mechanical effect of the sudden great increases in blood pressure, but other factors too may play a role. Arteriolonecrosis found in malignant hypertension allows therefore to conclude not the patient in which hypertension had developed and to the extreme height of blood pressure, but the vessels should be drawn from these changes as to different genesis of benign and malignant hypertension. Any disease associated with a rapidly developing hypertension may give rise to arteriolonecrosis. It is therefore more correct to use the term malignant hypertension syndrome, than to consider the conditions as a separate entity.

(iii) Arteriolonecrosis may develop into hyaline in a few days. It is for this reason that in some cases appearing clinically in the form of malignant hypertension little or no necrosis is present in the arteries only hyaline or an association of both changes.

(iv) Hypertension may lead to primary myocardial lesions resembling those occurring in the media of arteries, even without changes being present in the heart's own vessels.

Glomerulosclerosis: Gy. Róna (1st Dept. of Pathological Anatomy and Exp. Cancer Res. Budapest University Medical School)

Since the so called Kimmelstiel bodies, i. necrotic and hyalinized glomerular globules, characteristic of the nodular form of intercapillary glomerulosclerosis may occur also in mesangial, basement membrane, subendothelial glomerulonephritis, pyelonephritis, and subacute bacterial endocarditis, cannot be considered as specific for diabetes.

In 70 cases of diabetes was the problem examined, which is the role of the nodules in development of Kimmelstiel-Wilson's syndrome. It could be established that the nodular changes were not always accompanied by classical clinical symptoms. On the other hand, nodes may associate with nephrosis or hypertension without the podules being present. Correlation was found between the occurrence of nodules and the severity of clinical symptoms, even in forms of glomerulosclerosis attended by glomerular necrosis, when symptoms were more marked than in other cases.

Béla Róna and Kerekes have found that in diabetics capillary and arteriolar changes involving the glomerular lesion occur throughout the whole organism in the form of fibrillar necrosis and hyalinosis. Out of 42 cases of diabetes unaccompanied by glomerulosclerosis 5 were marked by necrosis of the arterial wall and in all but 4 cases was a varying degree of generalized hyalinosis of the arterioles present.

The Kimmelstiel body is not the cause of the clinical symptoms. It only indicates a lesion of the glomerular filter and an increased permeability and, together with the generalized necrosis and hyalinosis of the arterioles and with the clinical symptoms, it is a sequel of the general diabetic disorder.

The experimental results are also supporting this opinion. Glomerulosclerosis produced the rabbit by urethane is associated with severe albuminuria which, however, ceases after discontinuation of the drug. Whereas albuminuria is reversible, the glomeruli formed do not regress and remain easily demonstrable. Similar observations were made in glomerulosclerosis produced by carbonate in rabbits.

The Effect of Urethane on the Glomeruli of Various Experimental Animals:
Kerekes, Gy. Róna (1st Dept. of Pathological Anatomy and Exp. Cancer Res. of Budapest University Medical School)

The effect of urethane on glomerular capillaries was observed in 30 rabbits, 10 dogs, 10 guinea pigs, 20 rats and 20 mice. Each animal was given every second day 0.5 g/kg. of a 10 per cent solution of the substance intraperitoneally. 10 rabbits, and the same number of guinea pigs and mice, were treated with the double quantity of the drug. 10 controls in each group served as controls.

The experiments have shown that the reaction of glomerular capillaries to urethane differs with the animal species. In rabbits, glomerulonephritis, marked glomerular necrosis and hyalinization were developed whilst no inflammatory reaction occurred, i. e. changes analogous with intercapillary glomerulosclerosis appeared. In dogs the drug gave rise to intercapillary glomerulonephritis. Guinea pigs reacted with glomerular necrosis, focal hyalinization, intra- and extraglomerular cell proliferation. In acute experiments on rats and mice glomerular necrosis was observed to develop. An increase in the dose of urethane caused no difference in the type and severity of the changes.

The results show that other factors too than the toxic effect of urethane should be considered for the glomerular lesion. The central nervous system of the animals however, is severely damaged. In acute experiments, intense hypertension of the cortex and the basal ganglia appeared, not infrequently leading to stasis, perivascular destructive hemorrhages. In chronic experiments hyalinosis of the arterioles and their obliteratio often resulted in ischemic necrosis. Besides these morphological changes the reaction types of the animals also underwent a change. Therefore in the development of vascular and glomerular lesions a significant role must undoubtedly be attributed to the central nervous system.

Urethane may, through the mediation of the central nervous system, change morphological correlations. It may give rise to hypertrophy and fatty metaplasia in the adrenal cortex, due to overproduction of cortical hormones and exert in this way a decisive influence on the reaction of the glomeruli and the arterioles. The fact that the vascular changes were different in the various animals is due to the difference in the reaction type of their central nervous system.

DOCTORAL WORKS IN MEDICAL SCIENCE

On the Submicroscopic Structure of Fibroid Degeneration: K. John (Dept. of Pathological Anatomy of Penn University Medical School)

It was studied by means of polarization analysis whether in the so-called fibroid degeneration an actual fibroid inhibition is present. Differences between fibrin and collagen can be observed on the ground that the double refraction of collagen ceases after treatment with phenol to negative. The inversion of this optic property occurs at a definite phenol concentration, allowing to obtain a characteristic curve. At the same time, the double refraction of fresh and old fibrin remains unchanged after treatment with phenol.

By means of plotting the phenol concentration curve in the fibroid areas, it was found that pregnancy fibrin is pure fibrin, as also the fibroid changes of the bursae, ganglia, and the vascular walls consist of fibrous inhibition precipitated in the connective tissue. On the other hand, the fibroid occurring in rheumatic affection of the connective tissue, further in peptic ulcer, yielded a phenol concentration curve characteristic of pure collagen without any fibrin. From this fact it may be inferred that the molecular structure of the collagen has not changed in the course of these phenomena.

It is concluded that in those cases the two features of fibroid change, i.e. the swelling and the shift of the isobirefringent point toward the neutral one may be related to, and interpreted by, the change in the correlation between micellar structure and basic substance.

Changes in the Argyrophilic Fibre Meshwork of the Cerebral Veins under Experimental and Pathological Conditions: F. Billroth, I. Fallos (Dept. of Anatomy, Histology and Embryology of Budapest University Medical School)

In this stage of our studies on the argyrophilic fibres in cerebral vessels, congested and tumorous brains were examined.

Cerebral congestion was produced in cats and rats by ligation of the jugular veins. Human brains originating from cases with cardiac congestion were also examined. From among brain tumours, meningioma, carcinoma and sarcoma, meningocele, astrocytoma, and multiform glioma, etc. were studied.

The perivascular argyrophilic fibres in the various parts of the brain, such as the cortex, the white matter, stem ganglia, hypothalamus, were impregnated according to Pardau, Senniger and Blochowitsky. All the impregnable perivascular connective tissue fibres were taken into consideration. The following results were obtained.

(I.) In the brain of cats, rats, rabbits, and man, under normal conditions an argyrophilic meshwork can be demonstrated around the vessels.

(II.) In congestion, changes occur in the perivascular argyrophilic fibres. In marked congestion the meshwork is replaced by a parallel arrangement of the fibres. In gross congestion aggregation of the fibres to thick strands occur. In some areas the fibres increase in number.

(III.) In all tumorous brains examined there occurred an increase in the number of fibres. The highest degree of increase occurred in metastatic carcinoma. In areas displaying an increase in the number of fibres, fibre aggregated into thick strands appeared. These changes also bear some relation to the pathological circulatory conditions prevailing in the tumour.

The Role of Connective Tissue in the Pneumatization of the Petrous Part of the Temporal Bone: Gy. Márta (2nd Dept. of Pathological Anatomy of Budapest University Medical School)

It had been observed previously that pneumatization of the petrous bone takes place with the active partaking of connective tissue. During the later (second) phase of the first period of pneumatative activity the vessels are surrounded by proliferating connective tissue which, progressing up to the border of the fatty marrow spaces, opens the wall by the aid of osteoclasts and compresses the fatty marrow to the side. The epithelium of the central sinous body forms the lining of these preformed spaces. In intense fibrosis of the connective tissue the pneumatization activity ceased in that period. Similarly, the postoperative reproductive pneumatization also failed to occur when intense fibrosis was developing in the connective tissue. The varieties of pneumatization are due to several causes but one of the most important aetiological factors is the contraction of connective tissue. The inhibition of pneumatization is due to two pathological mechanisms: (I) the failure of the primary red marrow to transform into yellow marrow in early infancy and (II) the fibrotic connective tissue fails to allow new that pneumatization performing activity in early childhood. On basis of the present studies it is shown that

There is no evidence membrane constituents to be made responsible for the evolution of pneumatization type, since both at autopsy and at operation numerous petrous bones were met with in which an abscess occurring in early infancy had been followed by very active destruction and in some cases the extensive pneumatization was already fully developed at the time of autopsy. From among the aetiological factors whose role should undoubtedly be referred to inflammation, provided that it had repeatedly been occurring or it had lasted a very long time together with suppuration, giving rise to fibrosis and to a consequent reduction of the activity of connective tissue. It seems unavoidable to assume constitutional and genetic factors all the more since pneumatization on the two sides of the same person usually shows great differences. Observations made on children have shown that though in infarctus otitis may have occurred at an identical age, pneumatization may still be different. Examination of 600 petrous bones partly at autopsy and partly with biopsy has shown that lasting suppurations with or without formation of pseudotuberculosis, result in a considerable inhibition of pneumatization. After removal of such lasting purulent inflammation the relation was never significant and in these cases no masked fibrosis occurred. The relationship pneumatization may thus be brought into a causal relationship with inflammation. This relationship, however, must not be generalized, it being only valid if inflammation is being ended by fibrosis.

Blood Circulation in the Brain and Cerebral Tumours

J. Kiss, Gy. Tuglai (Dept. of Anatomy and Gynaecology No. 1 of Budapest University Medical School)

The authors demonstrate the special regulatory apparatuses found in the precapillary arterioles of human brain. The mechanism of Kiss' occlusion apparatus is also demonstrated. Simultaneously with the presentation of the nerve of the precapillary arteries they point out the fact that the occlusion apparatuses under consideration are supplied by nerves twisting around them which derive from other sources than the own nerve plexus of the small vessels. Thus, the occlusion apparatuses have a rich and, to some extent, independent innervation of their own. In these nerve plexuses local multipolar ganglion cells are also present.

They present the nerves of intracerebral arterioles, further Boeke-Schäfer's ground plexus (primal reticular) located upon the walls of these small arterioles.

Then the wide arterio-venous anastomoses situated before the praeapillaries are shown. These disorders play a prominent part in the disturbances of cerebral circulation and consequently in the toxicemic cerebral changes also. The spastic-ataxic syndrome described by Miller-Rucker is related to the occlusion apparatuses. The development of this syndrome is promoted by the onset of venous re-circulation resulting in a congestion due to the dilatation post-capillary veins.

Luminescence microscope carried out with toxemic brains can, by the colour difference induced by the stain, state the time of protein escape i.e. the age of the protein. The histological processes manifesting themselves in colour differences are very likely due to the denaturation of proteins the affinity of which to fluorescent dyes hardly increases.

Having used the same procedure in all cases, they found that the sections stained identically if the disease belonged to the same group, whilst diseases belonging to different groups are characterized by different staining of the sections.

Starting from the pictures obtained from various cases, the authors have concluded that the cases of encephalitis without convulsions cerebral edema prevails, whereas in cerebrovascular brain swelling is predominating. In the first case, attacks fail to occur because of the rapid development of edema. In convulsive encephalitis, the changes in nerve cells, their pathological discharge result in epileptiform convulsion attacks.

Scleroderma and Sclerosis : P. Balogh and J. Balog (1st Dept. of Pathological Anatomy and Exp. Cancer Res. of Budapest University Medical School)

Diffuse scleroderma belongs to the group of the so-called collagen disease. Its aetiology unknown. Two cases are demonstrated, both of them displaying pituitary changes to which aetiological role could be attributed. In the first case, that of a woman of 19 years, a cyst filled with oilseed was found between the two lobes of the hypophysis. The cyst, measuring by 12 by 10 mm, compressed the posterior lobe. In the second case, a 34 years old woman had been operated on for diffuse scleroderma, died soon after the operation. The pituitary

of the hypophysis was found to pass through the anterior lobe and a second one, longer, one occurred also behind the pituitary. No pituitary was present in the animal. The changes disturbed the neuroendocrine function of the hypophysis and gave rise to a severe syndrome.

Hardening of the skin in infants is called sclerema. This condition is rather frequent. Several morbid conditions of different aetiology and type belong to it. In a case of aged 14 months the condition had set in at the age of 3 months. Simultaneously with the progressive hardening, appeared on the skin finally to extend all over the body. In this way the skin became indurated and tight. Administration of mineral salicylates and cortisone had no effect. Death occurred with clonic seizures. The fat tissue was swollen, vascularized and showed fluent necrotic and inflammatory foci. The same changes as in the subcutaneous fat were found in the mesenteral and perirenal fat tissue, etc. In the brain perivascular lymphocytic infiltration, sclerosis in the vessels, and cells containing fat globules in the myelin sheath were present. The disease resembles subcutaneous fat necrosis and Wohlfahrt's choriomeningitis which consists in a relapsing, focal, febrile, non-purulent paroxysms. Sclerema described here, however, differs from both conditions owing to the changes of the nervous system.

Central Control of Gonadotrophic Pituitary Function through a Negative Feedback Mechanism of Ovarian Hormone Production; R. Fuchs (Dept. of Anatomy of Pez University Medical School)

If the feedback mechanism induced by the ovarian blood flow is violated, the pituitary hypophysis was inhibited by implanting an ovary into the spleen of a castrated animal. A castrated female was implanted with an ovary into the spleen of a castrated animal. After the subcutaneous and increased production of FSH and LH resulted similarly as after the complete destruction of the supraoptical region of the hypothalamus. This can be best explained by the blood level of ovarian hormones.

The effect of protracted administration of big doses of follicular hormone, which in itself gives rise to ovarian atrophy, could be prevented by destroying the areas of the supraoptical region of the hypothalamus. The prevention manifested itself in the formation of a functioning corpus luteum whereas in the ovaries of unoperated animals treated for the same time with the same doses of follicular hormone, follicle formation was inhibited and no corpus luteum appeared.

The identical results of the two different experiments suggest that the production of gonadotrophic hormone in the anterior pituitary lobe is regulated by the supraoptical region through the inhibiting resp. stimulating nervous impulse which is started by the blood level of ovarian hormones and which regulates the production of gonadotrophic hormone in the pituitary gland through a neurohormonal feedback mechanism.

Inhibition of the Gastrogenous Effect by Focal Injury to the Epithalamus; B. Moos (Dept. of Anatomy of Pez University Medical School)

Experiments were performed with a rat strain in which on the effect of an unknown gasterogenous agent the thyroid displayed a change resembling thyroid gigantism. This disappeared after treating the rats with 10 micrograms of thyroxin daily for 20 days. A similar restitution could be attained by electrolytic destruction of the epithalamic region (and both sides) or of both sides). If the epithalamic lesion was followed by the thyroid treatment mentioned above a thoroughly normal histologic structure of the thyroid resulted. On the other hand, when a focal injury to the tuber cinereum could inhibit the stimulatory effect. The observations have been fully confirmed by a quantitative examination of the thyroids by means of Jacoby's nucleus variation statistics.

It is inferred from the results that the epithalamic region is the area of the central nervous system sensitive to the thyroxin level in the organism. This region would, according to the present knowledge, increase or lower thyroxin level in the serum, inhibit or stimulate, respectively, the production and excretion of the thyrotropic hormone of the pituitary gland.

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